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EXAMINER

PONNALURI, PADMASHRI

ART UNIT PAPER NUMBER

1639

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/057,632

Applicant(s)

BURCH ET AL.

Examiner

Padmashri Ponnaluri

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 38 and 47-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 38 and 47-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/19/05 has been entered.

### **Status of the Claims**

2. New claims 51-52 have been added by the amendment filed on 7-19/05. Claims 38 and 47-52 are currently pending and under consideration.

### ***Priority***

3. This application is continuation of 09/154,354, which claims priority to 60/059,195.

### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

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invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 38, 47-48, 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al. US Pat. No. 4,569,937 (2/86) and Tanaka et al (Arzneimittel-Forschung (1992) Vol. 42(7) pages 935-44).

The instant claim briefly recites a method of effectively treating pain in humans comprising orally administering to a human patient an oral dosage form comprising analgesic compounds consisting essentially of (i) N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl] methanesulfonamide and/or at least one pharmaceutically acceptable salt thereof; and (ii) oxycodone and/or at least one pharmaceutically acceptable salt thereof.

Baker et al. teach pharmaceutical compositions for relieving pain in humans comprising a combination of :a. a narcotic analgesic (preferably oxycodone: see formulations col. 4-8; patent claims), or a pharmaceutically acceptable salt thereof; and b. ibuprofen (a non-steroidal anti-inflammatory drug or NSAID: see col. 1-2), or a pharmaceutically acceptable suitable salt thereof, in a weight ratio of about 1:800 (e.g. .001:1) to 1:1 (compare to present claim 47: See col. 2) with oxycodone amounts of about 5 mgs-600mgs (compare to present claim 52).

The Baker reference teaches oral administration, which can be coadministered in a single dosage forms (e.g. see col. 3-8) or sequentially administered (e.g. col. 8-9 ; "... mice are dosed sequentially..."). The oral dosage forms include "sustained release" formulations (e.g. tablets, capsules, etc: see col. 3-4, especially col. 4). The Baker et al. reference teach that dose ratios can be adjusted and that the analgesic activity of the combined oxycodone and ibuprofen activity is "unexpectedly enhanced" or synergistic i.e. the resulting activity is greater than the activity

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expected from the sum of the activities of the individual components, thereby permitting reduced dosages of narcotic analgesics (e.g. oxycodone) AND which diminishes adverse side effects (e.g. addiction) and toxicity which would result from the otherwise required amounts of the individual drug components resulting from high dosages of oxycodone or NSAID's such as ibuprofen. See e.g. col. 1-2; col. 3, lines 19-32. Accordingly, Baker would teach the use of therapeutic and subtherapeutic amounts of oxycodone and/or ibuprofen in view of the additive or synergistic nature of the combinations and the desire to reduce the toxicity and/or side-effects of both agents; and as required by the doctor for his/her particular patient, including dosage optimization e.g. dosage overlapping of active ingredients. See e.g. col. 3 where dosage is modified to suit the particular patient.

Baker et al further teach in view of the test results of analgesic activities of oxycodone and ibuprofen, it is possible to predict the range of maximum potentiating dosages for man, and utilizing the data from the present invention and the equivalent ratios in man, it is predicted that oxycodone amounts and the ratio of the oxycodone and ibuprofen for the oral dosage in man (i.e., see columns 12-13).

The Baker analgesic composition differs from that presently claimed in that it fails to teach the substitution of T-614 (N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl) for ibuprofen into the Baker compositions.

Tanaka et al. teach that T-614 possesses superior analgesic potency, as compared to ibuprofen, against inflammatory pain and antigen-induced arthritic pain in rats with virtually no gastrointestinal ulcerogenic action and no affect on water/sodium excretion.

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Accordingly, one of ordinary skill in the art would have been motivated to substitute T-614 for ibuprofen in the Baker reference compositions in light of the Tanaka reference teaching that ibuprofen is more analgesically potent with less side effects (e.g. as compared to ibuprofen) in animal models .

Additionally, it is noted that the instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two (or more) compositions each of which is taught by the prior art to be useful for the same purpose

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Baker reference analgesic composition by substituting T-614 for ibuprofen in light of the benefits of T-614 (increased potency/decreased side effect as compared to ibuprofen) as taught by the Tanaka reference.

7. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baker et al, and Tanaka et al, as applied to claims 38, 47-48, 50-52 above, and further in view of US patent 5,472,712 (Oshlack et al) or US Patent 6,294,195 (Oshlack et al)

The substance of the above obviousness rejection is hereby incorporated by reference in its entirety.

Although the Baker reference teaches oral dosage forms which include "sustained release" formulations (e.g. tablets, capsules, etc: see col. 3-4, especially col. 4) utilizing "sustained release carriers", the Baker reference fails to explicitly teach "a sustained release carrier which provides a sustained release of the oxcodone and/or ... salt thereof".

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However, the use of sustained release dosage forms for opioid analgesics, including oxycodone which utilize sustained release carriers employing beads which are coated with the opioid drug or which include substrate layers which include the drugs is known in the art to effectuate delayed release of extended duration. E.g. see Oshlack et al. and Oshlack patent references.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize sustained release carriers for oxycodone including beads/layers as taught by the Oshlack and Oshlack et al. patents for use in the Baker compositions since Baker specifically teaches using "sustained release formulations" and further in view of the advantages of utilizing the Oshlack patent sustained release carriers including delayed drug release of extended duration.

### ***Response to Arguments***

8. Applicant's arguments filed on 7-19/05, regarding the rejection of claims over Baker et al, and Tanaka et al, have been fully considered but they are not persuasive.

Applicant's arguments regarding the rejections have been addressed in the advisory office

action mailed on 6/14/05, which is hereby incorporated by reference in its entirety.

Applicants further argue that one skill in the art would not be motivated to substitute the ibuprofen of formulations of Baker et al with N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl] methanesulfonamide (T-614) of Tanaka et al.

Applicants arguments have been considered and are not persuasive because 'the examiner recognizes that obviousness can only be established by combining or modifying the teachings of

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the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In the present case, the above rejection provides ample motivation to combine the references *inter alia* the substitution of one non-narcotic NSAID for another, especially where the secondary reference suggests benefits imparted by making the substitution as outlined in the rejection above.

Additionally, as pointed out in the above rejection, it is noted that the instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two (or more) compositions each of which is taught by the prior art to be useful for the same purpose.

And Substituting one functionally equivalent compound for another (e.g. non-opioid NSAID's ie. Cox inhibitors) to treat inflammatory pain is directly in line with sound scientific reasoning and established case law including *In re Kerkhoven* cited above.

Applicant's interpretation of the Baker patent reference fails to consider the Baker patent teaching as a whole to one of ordinary skill in the art.

The Baker teaching includes Baker's entire specification and claims, inclusive of Baker's summary of the state of the prior art as illustrated in the "The Background of the Invention" (col. 1-2). In this respect, Baker '936 (col. 1-2) cites numerous prior art references starting with Sunshine et al. for the premise of making analgesic compositions by combining NSAID's with narcotic analgesic (distinguished by merely additive analgesic effect) as well as other NSAIDS's (e.g. acetaminophen etc) with various narcotic analgesics, most notably oxycodone. Baker's



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invention (e.g. following the summary) is distinguished from the prior art by selecting compositions comprising ibuprofen as the NSAID in combination with narcotic analgesics (including oxycodone) in synergistically effective amounts while reducing the amounts of the narcotic analgesic thus addressing the problem of addiction (pointed to at the end of the "Background of the Invention").

In light of the "Background of the Invention" and lack of any evidence that substitution with a different NSAID would render pain treatment inoperative applicant's teaching away argument is not understood. At most, the selection of a different NSAID may lead to less than synergistic pain relief (e.g. additive) and as such may be "less preferred". In this regard, however, it is noted that:

Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). See also MPEP 2121.04.

Accordingly, for the reasons recited above and for the reasons already of record, the obviousness rejections of record are hereby maintained.

9. Applicant's arguments filed on 7/19/05 regarding the rejection of claim 49 over Baker et al, Tanaka et al and Oschlack et al, have been fully considered but they are not persuasive.

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Applicants argue that Oshlack et al reference do not cure the deficiencies of the Baker reference in view of the Tanaka et al and Oschlack et al. Applicant's arguments have been considered and are not persuasive for the reasons discussed supra.

***Conclusion***

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
PADMASHRI PONNALURI  
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